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LETTER TO THE EDITOR

Cefepime-induced encephalopathy

The most common adverse event of cefepime on the central nervous system is seizure.[1] Cefepime induced encephalopathy, however, has been only rarely reported.[2,3]

A 60-year-old diabetic patient with end stage renal disease on hemodialysis was admitted with left pleuritic chest pain and productive cough. He was afebrile and hemodynamically stable, with a systolic apical heart murmur, bilateral basal lung crackles, and hepatomegaly. Laboratory data: Hemoglobin 10.4 g/dl, Hematocrit 32%, WBCs 11000/mm^3, PMN's 91%, creatinine 10.9 mg/dl and BUN 64 g/l. Chest film showed right middle lobe infiltrates and cefepime (2 g/d) was started empirically. Five days later, the patient started to show confusion, have visual and auditory hallucinations, and agitation with no focal deficit on physical examination. These neurological symptoms did not improve upon further dialysis over two days; cefepime was then stopped. Within one day, he started to improve, and two days later, he returned to his baseline level of mental status. Upon re-interviewing his wife and reviewing his medical record, he was found to have had hallucinations and confusion after taking ceftazidime, a year earlier.

Cephalosporin induced neurotoxicity has been reported with ceftazidime, ceftriaxone, and cefuroxime.[4–6] The main predisposing factors are pre-existing CNS abnormalities and renal impairment with excessive dosing of the antibiotic.[7]

Our patient was given two grams of cefepime daily based on recommendations of Gilbert et al.[8] He developed confusion, hallucinations and agitation, which progressed over one week despite intensification of hemodialysis and the absence of electrolyte disturbances. Cefepime was then stopped due to circumstantial evidence and the previous occurrence of hallucinations with ceftazidime the year before. A CT scan of the brain was not requested due to the lack of focal motor or sensory deficit, and an EEG was not carried out because of the rapid clinical improvement after stopping cefepime.

Neurotoxicity of cefepime has been reported before and the spectrum of manifestations has been broad including: confusion, hallucinations, agitation, convulsions, tremor, delirium and coma (Table 1). The latency of neurotoxicity, which is the period between the start of cefepime treatment and neurologic manifestations, varied between one and ten days, and all neurological symptoms regressed within two to seven days after stopping the antibiotic infusion. Almost all patients affected have had renal failure and the dose of cefepime was relatively high for the level of renal failure. The newer Sanford guides to antimicrobial therapy (2001 to 2003) suggest a smaller dose of cefepime according to the creatinine clearance.[11] Thus, if a patient on cefepime develops neurological symptoms, drug neurotoxicity should be considered.

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Table 1 Cases of cefepime induced neurotoxicity reported in the literature.

Study	Year	Age (Year)	Sex	Cefepime dose	RF	Number of cases	Clinical findings	Diagnosis	Latency (days)	Treatment
Fishbain et al.[2]	2000	74	F	2 g/24 h	Yes	1	Confusion, delirium, coma	EEG*, drug level	4	D/C AB
Jallon et al.[3]	2000	57—91	7M/12F	2—6 g/24 h	Yes	19	Confusion, hallucination	EEG*	1—7	D/C AB
Martinez-Rodriguez et al.[6]	2001	54—86	3M/3F	1—2 g/24 h	Yes	6	Agitation, confusion, myoclonus,	EEG*	1—10	D/C AB, Clonazepam, phenytoin
Chetaille et al.[9]	1997		F	3 g/24 h	Yes	1	Confusion, convulsion	EEG**		D/C AB
Dixit et al.[10]	2000	44/28	M/F	2 g/24 h	Yes	2	Confusion, tremor, hyperreflexia, seizure	EEG***	1	D/C AB

M: male, F: female, h: hour, *: triphasic wave encephalopathy, **: irritative state, ***: continuous generalised sharp wave with slow activity, RF: renal failure, D/C: discontinuation of drugs, g: grams, h: hour, AB: antibiotic.

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